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=> fil hcaplu
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FILE COVERS 1907 - 25 Nov 2002  VOL 137 ISS 22
FILE LAST UPDATED: 24 Nov 2002  (20021124/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

CAS roles have been modified effective December 16, 2001. Please
check your SDI profiles to see if they need to be revised. For
information on CAS roles, enter HELP ROLES at an arrow prompt or use
the CAS Roles thesaurus (/RL field) in this file.

=> d stat que
L7            68 SEA FILE=REGISTRY (10238-21-8/BI OR 103775-10-6/BI OR 109214-55
                 -3/BI OR 110703-94-1/BI OR 111025-46-8/BI OR 111223-26-8/BI OR
                 11128-99-7/BI OR 112733-06-9/BI OR 112808-22-7/BI OR 114798-26-
                 4/BI OR 1156-19-0/BI OR 122320-73-4/BI OR 129688-50-2/BI OR
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                 OR 93479-97-1/BI OR 93957-54-1/BI OR 97322-87-7/BI OR 98048-97-
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L8             2 SEA FILE=REGISTRY L7 AND PYRIMID?
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L11            7 SEA FILE=REGISTRY (TROGLITAZONE/CN OR "TROGLITAZONE DIHYDRATE"/
                 CN OR "TROGLITAZONE GLUCURONIDE"/CN OR "TROGLITAZONE METABOLITE
                  A"/CN OR "TROGLITAZONE METABOLITE B"/CN OR "TROGLITAZONE
                 QUINONE"/CN OR "TROGLITAZONE SULFATE"/CN OR "TROGLITAZONE
                 SULFATE ESTER"/CN)
L12            3 SEA FILE=REGISTRY (ROSIGLITAZONE/CN OR "ROSIGLITAZONE MALEATE"/
                 CN OR "ROSIGLITAZONE NITRATE"/CN)
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Searched by M. Smith

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                N OR "GLIBENCLAMIDE-.BETA.-CYCLODEXTRIN COMPLEX (1:2)"/CN OR
                "GLIBENCLAMIDE-GLUCOSE MIXTURE"/CN OR "GLIBENCLAMIDE-PHENFORMIN
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                1:1 SALT"/CN)
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L19           6 SEA FILE=REGISTRY (METFORMIN/CN OR "METFORMIN CLOFIBRATE"/CN
                OR "METFORMIN HYDROCHLORIDE"/CN OR "METFORMIN OROTATE"/CN OR
                "METFORMIN PAMOATE"/CN OR "METFORMIN TOLBUTAMIDE SALT"/CN)
L20           2 SEA FILE=REGISTRY (ACARBOSE/CN OR "ACARBOSE 7-KINASE"/CN)
L21           1 SEA FILE=REGISTRY REPAGLINIDE/CN
L23      146762 SEA FILE=HCAPLUS L10 OR INSULIN
L24        1146 SEA FILE=HCAPLUS L11 OR TROGLITAZONE
L25         621 SEA FILE=HCAPLUS L12 OR ROSIGLITAZONE?
L26         576 SEA FILE=HCAPLUS L13 OR PIOGLITAZONE?
L27          32 SEA FILE=HCAPLUS L14 OR MCC(W)555
L28         216 SEA FILE=HCAPLUS L15 OR GLIMEPIRIDE?
L29        4718 SEA FILE=HCAPLUS L16 OR GLIBENCLAMIDE?
L30         515 SEA FILE=HCAPLUS L17 OR GLICLAZIDE?
L31         316 SEA FILE=HCAPLUS L18 OR TOLAZAMIDE?
L32        1472 SEA FILE=HCAPLUS L19 OR METFORMIN
L33         799 SEA FILE=HCAPLUS L20 OR ACARBOSE?
L34         184 SEA FILE=HCAPLUS L21 OR REPAGLINIDE?
L36      152411 SEA FILE=HCAPLUS L23 OR L24 OR L25 OR L26 OR L27 OR L28 OR L29
                OR L30 OR L31 OR L32 OR L33 OR L34
L37          16 SEA FILE=HCAPLUS L9 AND L36
L38          12 SEA FILE=HCAPLUS L37 AND DIABET?


=> d ibib abs hitrn l38 1-12

L38  ANSWER 1 OF 12  HCAPLUS  COPYRIGHT 2002 ACS
ACCESSION NUMBER:         2002:813924  HCAPLUS
DOCUMENT NUMBER:          137:311200
TITLE:                    Preparation of 2,1-oxazoline and 1,2-pyrazoline-based
                          inhibitors of dipeptidyl peptidase IV

INVENTOR(S):              Sulsky, Richard B.; Robl, Jeffrey A.
PATENT ASSIGNEE(S):       Bristol-Myers Squibb Company, USA
SOURCE:                   PCT Int. Appl., 61 pp.
                          CODEN: PIXXD2

DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE          APPLICATION NO.  DATE
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     WO 2002083128      A1   20021024      WO 2002-US10936  20020405
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
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GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,
TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.: US 2001-283438P P 20010412
OTHER SOURCE(S): MARPAT 137:311200
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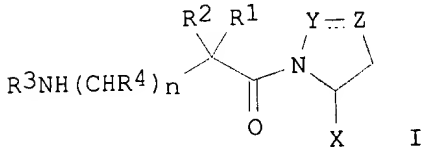

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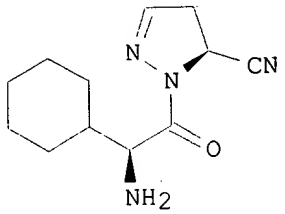


II

AB The invention describes dipeptidyl peptidase IV (DP 4) inhibiting compds. I [n is 0 or 1; X is H or CN; Y is N, NH or O; Z is CH2 when Y is O or NH, with Y-Z forming a single bond, and Z is CH when Y is N, with Y-Z forming a double bond; R1-R4 = H, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, bicycloalkyl, bicycloalkylalkyl, alkylthioalkyl, arylalkylthioalkyl, cycloalkenyl, aryl, aralkyl, heteroaryl, heteroarylalkyl, cycloheteroalkyl or cycloheteroalkylalkyl, which may be substituted; R1 may combine with R3 or R4 to form a ring (CR5R6)2-6 or (CR7R8)3-6, resp., where R5-R8 = H, OH, alkoxy, alkyl, aryl, etc.] and their pharmaceutically-acceptable salts or prodrug esters. A method is also provided for treating **diabetes** and related diseases, employing a DP 4 inhibitor I, optionally in combination with other therapeutic agents, including an antidiabetic, hypolipidemic, or anti-obesity agent. Thus, coupling of sultam-protected 1,2-pyrazoline-3-carboxamide with (S)-N-(tert-butoxycarbonyl)cyclohexylglycine (HOAt, Et3N, and EDAC in CH2Cl2), followed by sultam cleavage with methanolic ammonia, amide conversion to nitrile using imidazole, and deprotection, afforded II.TFA.

IT **657-24-9, Metformin 9004-10-8, Insulin**
, biological studies **10238-21-8,** Glyburide **21187-98-4,**
Gliclazide 56180-94-0, Acarbose
93479-97-1, Glimepiride 97322-87-7,
Troglitazone 111025-46-8, Pioglitazone
122320-73-4, Rosiglitazone 135062-02-1,
Repaglinide
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antidiabetic agent; prepn. of oxazoline and pyrazoline-based inhibitors of dipeptidyl peptidase IV)

Searched by M. Smith

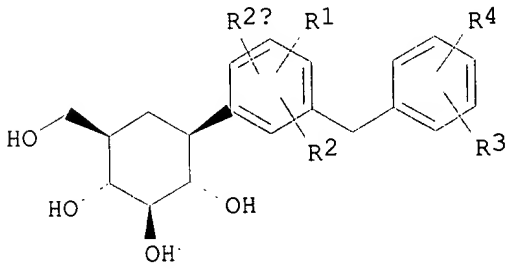
IT **287714-41-4**, Rosuvastatin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lipid modulating agent; prepn. of oxazoline and pyrazoline-based inhibitors of dipeptidyl peptidase IV)
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 2 OF 12 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:813874 HCAPLUS
DOCUMENT NUMBER: 137:311199
TITLE: Amino acid complexes of C-aryl glucosides for treatment of **diabetes**
INVENTOR(S): Gougoutas, Jack Z.
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 80 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002083066	A2	20021024	WO 2002-US11066	20020408

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-283097P P 20010411
OTHER SOURCE(S): MARPAT 137:311199
GI



I

AB Cryst. complexes are obtained from 1:1 or 2:1 mixts. of either the (D) or (L) enantiomer of natural amino acids and compds. of formula I [R1, R2, R2a = H, OH, OR5, alkyl, OCHF2, OCF3, SR5a, halogen; R3, R4 = H, OH, OR5b, alkyl, cycloalkyl, CF3, OCHF2, OCF3, halogen, CONR6R6a, CO2R5c, CO2H, COR6b, CH(OH)R6c, CH(OR5d)R6d, CN, NHCOR5e, NHSO2R5f, NHSO2-aryl, SR5g, SOR5h, SO2R5i, or a five, six or seven membered heterocycle which may contain 1 to 4 heteroatoms (N, O, S, SO, and/or SO2), or R3 and R4 together with the carbons to which they are attached form an annelated

five, six or seven membered carbocycle or heterocycle which may contain 1 to 4 heteroatoms in the ring; R5, R5a-R5i are independently alkyl; R6, R6a-R6d are independently H, alkyl, aryl, alkylaryl or cycloalkyl, or NR6R6a form an annelated five, six or seven membered heterocycle which may contain 1 to 4 heteroatoms in the ring]. A method is also provided for treating **diabetes** and related diseases employing an SGLT2 (sodium dependent glucose transporters found in the intestine and kidney) inhibiting amt. of the above complex alone or in combination with another antidiabetic agent or other therapeutic agent. Thus, I (R1 = 4-Me, R4 = 4-OCHF2, R2, R2a, R3 = H) was prepd. by a multistep procedure starting from o-toluic acid, anisole, 2,3,4,6-tetra-O-benzyl-.beta.-D-glucolactone, and CHF2Cl and treated with L-phenylalanine to form the cryst. 1:1 complex.

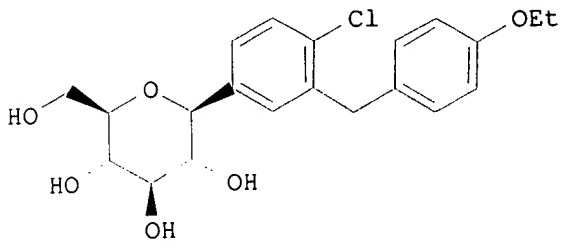
IT **657-24-9, Metformin 9004-10-8, Insulin**, biological studies **10238-21-8,** Glyburide **21187-98-4, Gliclazide 56180-94-0, Acarbose 93479-97-1, Glimepiride 97322-87-7, Troglitazone 111025-46-8, Pioglitazone 122320-73-4, Rosiglitazone 135062-02-1, Repaglinide 287714-41-4,** Rosuvastatin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of amino acid/C-aryl glucoside complexes for treatment of **diabetes** and related diseases)

L38 ANSWER 3 OF 12 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:736927 HCAPLUS
DOCUMENT NUMBER: 137:247879
TITLE: Preparation of antidiabetic agents C-aryl glucoside as human SGLT2 inhibitors
INVENTOR(S): Ellsworth, Bruce; Washburn, William N.; Sher, Philip M.; Wu, Gang; Meng, Wei
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 17 pp., Cont.-in-part of U.S. 6,414,126.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002137903	A1	20020926	US 2002-151436	20020520
US 6414126	B1	20020702	US 2000-679027	20001004

PRIORITY APPLN. INFO.:
US 1999-158773P P 19991012
US 2000-194615P P 20000405
US 2000-679027 A2 20001004

GI



I

AB An SGLT2 inhibiting compd. is provided having the formula I method is also provided for treating **diabetes** and related diseases employing an SGLT2 inhibiting amt. of the above compd. alone or in combination with another antidiabetic agent or other therapeutic agent (no data). 1A pharmaceutical combination comprising an SGLT2 inhibitor compd. and an antidiabetic agent other than an SGLT2 inhibitor, for treating the complications of **diabetes**, an anti-obesity agent, an antihypertensive agent, an antiplatelet agent, an antiatherosclerotic agent, and/or a lipid-lowering agent (no data). A method for treating or delaying the progression or onset of **diabetes**, **diabetic** retinopathy, **diabetic** neuropathy, **diabetic** nephropathy, delayed wound healing, **insulin** resistance, hyperglycemia, hyperinsulinemia, elevated blood levels of fatty acids or glycerol, hyperlipidemia, obesity, hypertriglyceridemia, Syndrome X, **diabetic** complications, atherosclerosis or hypertension, or for increasing high d. lipoprotein levels, which comprises administering to a mammalian species in need of treatment a therapeutically effective amt. of a compd (no data).

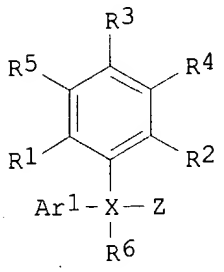
IT **657-24-9, Metformin 9004-10-8, Insulin**, biological studies **10238-21-8**, Glyburide **21187-98-4, Gliclazide 56180-94-0, Acarbose 93479-97-1, Glimepiride 97322-87-7, Troglitazone 111025-46-8, Pioglitazone 122320-73-4, Rosiglitazone 135062-02-1, Repaglinide 287714-41-4**, Rosuvastatin
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of antidiabetic agents C-aryl glucosides as human SGLT2 inhibitors)

L38 ANSWER 4 OF 12 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:637483 HCAPLUS
DOCUMENT NUMBER: 137:185311
TITLE: Preparation of 2-aryloxy-2-arylalkanoic acids for **diabetes** and lipid disorders
INVENTOR(S): Adams, Alan D.; Jones, A. Brian; Berger, Joel P.; Dropinski, James F.; Elbrecht, Alexander; Liu, Kun; Macnaul, Karen Lamb; Shi, Guo-qiang; Von, Langen Derek J.; Zhou, Gaochao
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 157 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002064094	A2	20020822	WO 2002-US4680	20020205

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,

CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.: US 2001-267809P P 20010209
OTHER SOURCE(S): MARPAT 137:185311
GI



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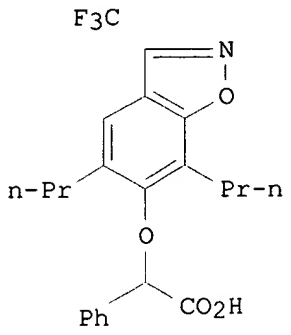


II

AB Title compds. I [R1 = halo, alkyl, alkoxy; R2 = alkyl, alicyclic; R3 = alkyl, aryl, alicyclic, heterocycle, etc.; R4 = H, OH, alkoxy, aryloxy, halo or R3-4 may be joined together to yield 5- or 6-membered heterocycle; R5 = H, halo; R6 = H, halo, CH3, CF3; Ar1 = Ph, thienyl, thiazolyl, oxazolyl, pyridyl; X = O, S; Z = COOH, tetrazole, carboxamide] were prepd. For instance, 2,4-dipropylresorcinol was converted to 2,4-dihydroxy-3,5-dipropyl-.alpha.,.alpha.,.alpha.-trifluoroacetophenone (CH2Cl2, TFAA, AlCl3) and subsequently treated with i. hydroxylamine.bul.HCl, MeOH, reflux; ii. Ac2O; iii. pyridine, reflux which afforded 5,7-dipropyl-6-hydroxy-3-trifluoromethyl-1,2-benzisoxazole. The benzisoxazole was reacted with Me 2-bromo-2-phenylacetate (DMF, Cs2CO3) and the product sapond. to give II. I are potent agonists of the peroxisome proliferator activated receptor and are useful in the treatment of non-**insulin** dependent **diabetes** mellitus (NIDDM), hyperglycemia, dyslipidemia, hyperlipidemia, hypercholesterolemia, hypertriglyceridemia, atherosclerosis, obesity, vascular restenosis, inflammation, and other PPAR-.alpha. and/or PPAR-.gamma. mediated diseases.

IT **657-24-9**, **Metformin 56180-94-0**, **Acarbose 97322-87-7**, **Troglitazone 111025-46-8**, **Pioglitazone 122320-73-4**, **Rosiglitazone 147098-20-2**, ZD-4522 **161600-01-7**, **MCC-555**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination pharmaceutical; prepn. of 2-aryloxy-2-arylalkanoic acids for **diabetes** and lipid disorders)

IT **9004-10-8**, **Insulin**, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(resistance; prepn. of 2-aryloxy-2-arylalkanoic acids for **diabetes** and lipid disorders)

L38 ANSWER 5 OF 12 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:594636 HCAPLUS
DOCUMENT NUMBER: 137:135097
TITLE: Acyl sulfamides for treatment of obesity, **diabetes** and lipid disorders
INVENTOR(S): Jones, A. Brian; Acton, John J., III

PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 64 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002060388	A2	20020808	WO 2002-US3119	20020125

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-264955P P 20010130
OTHER SOURCE(S): MARPAT 137:135097

AB A class of acyl sulfamides comprises compds. that are potent ligands for PPAR.gamma. receptors and generally have antagonist or partial agonist activity. The compds. may be useful in the treatment, control or prevention of obesity, non-**insulin** dependent **diabetes** mellitus (NIDDM), hyperglycemia, dyslipidemia, hyperlipidemia, hypercholesterolemia, hypertriglyceridemia, atherosclerosis, vascular restenosis, inflammation, and other PPAR.gamma. receptor-mediated diseases, disorders and conditions, alone or in combination with one or more other compds. Other compds. are selected from **insulin** sensitizers, **insulin** or **insulin** mimetics, sulfonylureas, .alpha.-glucosidase inhibitors, cholesterol lowering agents, PPAR.delta. agonists, antiobesity compds., an ileal bile acid transporter inhibitor, and agents intended for use in inflammatory conditions such as aspirin, nonsteroidal anti-inflammatory drugs, glucocorticoids, azulfidine, and cyclooxygenase-2 selective inhibitors.

IT **657-24-9**, **Metformin 56180-94-0**, **Acarbose 97322-87-7D**, **Troglitazone**, derivs. **111025-46-8**, **Pioglitazone 122320-73-4**, **Rosiglitazone 147098-20-2**, ZD-4522 **161600-01-7**, **MCC-555**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(acyl sulfamides and other drugs for treatment of metabolic disorders mediated by PPAR.gamma. receptors)

IT **9004-10-8**, **Insulin**, biological studies
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mimetics and sensitizers of and resistance to; acyl sulfamides and other drugs for treatment of metabolic disorders mediated by PPAR.gamma. receptors)

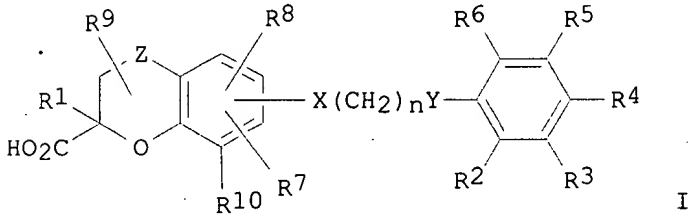
L38 ANSWER 6 OF 12 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:575765 HCAPLUS
DOCUMENT NUMBER: 137:140435
TITLE: Benzopyrancarboxylic acid derivatives with PPAR agonist activity for the treatment of **diabetes** and lipid disorders, and their preparation, pharmaceutical compositions, and use

INVENTOR(S): Sahoo, Soumya P.; Koyama, Hiroo; Miller, Daniel J.; Boueres, Julia K.; Desai, Ranjit C.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 42 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002103242	A1	20020801	US 2001-21667	20011029
WO 2002060434	A2	20020808	WO 2001-US49501	20011026

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-244698P P 20001031
OTHER SOURCE(S): MARPAT 137:140435
GI



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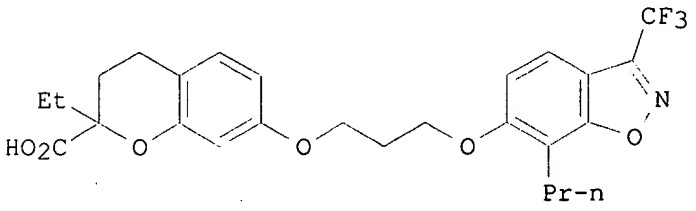


II

AB A class of benzopyrancarboxylic acid derivs. is disclosed, which comprises compds. that are potent agonists (no data) of peroxisome proliferator activated receptors (PPAR) alpha and/or gamma, and are therefore useful in the treatment, control, or prevention of non-**insulin** dependent **diabetes** mellitus (NIDDM), hyperglycemia, dyslipidemia, hyperlipidemia, hypercholesterolemia, hypertriglyceridemia, atherosclerosis, obesity, vascular restenosis, inflammation, and other PPAR alpha and/or gamma mediated diseases, disorders and conditions. In particular, compds. I and their pharmaceutically acceptable salts and/or

prodrugs are disclosed [wherein: Z = CH2, CO; R1 = H, OH, halo, (un)substituted alk(en/yn)yl, alk(en/yn)yloxy, or aryl; or R1 forms (un)substituted cyclopropane fusion to adjacent C atom; X, Y = O, S, SO, SO2, CH2, (un)substituted NH; n = 1-6; R4 = (un)substituted benzoheterocyclyl, cycloalkyl, heterocyclyl, cycloalkyloxy, halo, OH or derivs., alk(en/yn)yl, alk(en/yn)yloxy, or aryl, etc.; other R groups = H, halo, OH, (un)substituted alk(en/yn)yl, alk(en/yn)yloxy, aryl, aryloxy, aroyl, etc.; or R3R4 or R4R5 = (un)substituted 5- or 6-membered heterocyclic ring]. A list of 29 compds. is claimed, and their prepn. is described. For example, Et 7-hydroxy-4-oxo-4H-chromene-2-carboxylate underwent a sequence of: (1) complete hydrogenation of the enone (98%), (2) etherification of the alc. with PhCH2O(CH2)3Br (66%), (3) alpha ethylation of the ester (70%), (4) hydrogenolytic debenzylation (100%), (5) conversion of the resultant alc. to a bromide (96%), (6) etherification of the bromide with 3-(trifluoromethyl)-7-propyl-6-hydroxybenz[4,5]isoxazole (85%), and (7) alk. hydrolysis (100%), to give title compd. II. PPAR binding assays using human recombinant PPAR are described without data. Co-administration of compds. I with a variety of other drug categories, including a no. of specific drugs, is claimed.

IT **9004-10-8, Insulin**, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study) (resistance, treatment of; prepn. of benzopyrancarboxylic acid derivs. as PPAR agonists for treatment of **diabetes** and lipid disorders)

IT **657-24-9, Metformin 9004-10-8D, Insulin**, mimetics **56180-94-0, Acarbose 97322-87-7, Troglitazone 111025-46-8, Pioglitazone 122320-73-4, Rosiglitazone 147098-20-2**, ZD-4522 **161600-01-7, MCC-555**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (therapeutic compns. also contg.; prepn. of benzopyrancarboxylic acid derivs. as PPAR agonists for treatment of **diabetes** and lipid disorders)

L38 ANSWER 7 OF 12 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:540258 HCAPLUS
DOCUMENT NUMBER: 137:109267
TITLE: Preparation of benzoxepinopyridines as HMG-CoA reductase inhibitors
INVENTOR(S): Robl, Jeffrey A.; Chen, Bang-chi; Sun, Chong-qing
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 42 pp., Cont.-in-part of U.S. Ser. No. 875,155.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002094977	A1	20020718	US 2001-7407	20011204
US 2002013334	A1	20020131	US 2001-875155	20010606

PRIORITY APPLN. INFO.: US 2000-211595P P 20000615
US 2001-875155 A2 20010606
OTHER SOURCE(S): MARPAT 137:109267
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [X = O, S, SO, SO2, NR7; Z = HOCHCH2CH(OH)CH2CO2R3, 4-hydroxy-2-oxopyran-6-yl, etc.; n = 0, 1; R1, R2 = alkyl, arylalkyl, cycloalkyl, alkenyl, cycloalkenyl, aryl, heteroaryl, cycloheteroalkyl; R3 = H, alkyl, metal ion; R4 = H, halo, CF3, etc.; R7 = H, alkyl, aryl, alkanoyl, aroyl, alkoxycarbonyl, etc.; R9, R10 = H, alkyl], were prepd. as HMG CoA reductase inhibitors active in inhibiting cholesterol biosynthesis, modulating blood serum lipids such as lowering LDL cholesterol and/or increasing HDl cholesterol, and treating hyperlipidemia, hypercholesterolemia, hypertriglyceridemia and atherosclerosis (no data). E.g., a multistep synthesis of II is reported.

IT **657-24-9**, **Metformin 10238-21-8**, Glyburide
21187-98-4, **Gliclazide 56180-94-0**,
Acarbose 93479-97-1, Glimepride **97322-87-7**,
Troglitazone 111025-46-8, **Pioglitazone**
122320-73-4, **Rosiglitazone 135062-02-1**,
Repaglinide 287714-41-4, Rosuvastatin
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(coadministered agents; prepn. of benzoxepinopyridines as HMG-CoA reductase inhibitors for the treatment of hyperlipidemia, hypercholesterolemia, hypertriglyceridemia, atherosclerosis, and other disorders)

IT **9004-10-8P**, **Insulin**, preparation
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(sensitizers, resistance, coadministered agents; prepn. of benzoxepinopyridines as HMG-CoA reductase inhibitors for the treatment of hyperlipidemia, hypercholesterolemia, hypertriglyceridemia, atherosclerosis, and other disorders)

L38 ANSWER 8 OF 12 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:240561 HCAPLUS
DOCUMENT NUMBER: 136:257242
TITLE: Statins (HMG-CoA reductase inhibitors) as a novel type of immunomodulator, immunosuppressor and anti-inflammatory agent
INVENTOR(S): Mach, Francois
PATENT ASSIGNEE(S): Novimmune S.A., Switz.
SOURCE: PCT Int. Appl., 82 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002024194	A2	20020328	WO 2001-EP11485	20010919
WO 2002024194	C2	20020919		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US,

UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2002010521 A5 20020402 AU 2002-10521 20010919
PRIORITY APPLN. INFO.: US 2000-664871 A 20000919
WO 2001-EP11485 W 20010919

AB The present invention relates to methods of causing MHC-class II or CD40 mediated immunomodulation, immunosuppression and anti-inflammatory action, in a subject suffering from or susceptible of suffering from a condition involving inappropriate immune response, which comprises administering to the subject at least one statin, or a functionally or structurally equiv. mol., in an amt. effective to modulate MHC class II or CD40 expression in the subject. The present invention provides a new class of agents that reduce or repress T-lymphocyte activation mediated by class II or CD40 expression and consequently are capable of acting as immunomodulators and antiinflammatory agents.

IT **287714-41-4**, Rosuvastatin
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(statins (HMG-CoA reductase inhibitors) as immunosuppressor and antiinflammatory agents that modulate MHC-class II or CD40 expression inducible by interferon .gamma. and T-lymphocyte activation)

L38 ANSWER 9 OF 12 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:157564 HCAPLUS
DOCUMENT NUMBER: 136:205424
TITLE: Combinations of **insulin** secretion enhancer, HMG-CoA reductase inhibitors and acetylcholinesterase inhibitors
INVENTOR(S): Allison, Malcolm; Gatlin, Marjorie Regan
PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Novartis-Erfindungen Verwaltungsgesellschaft m.b.H.
SOURCE: PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002015892	A2	20020228	WO 2001-EP9586	20010820

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2002014952 A5 20020304 AU 2002-14952 20010820
PRIORITY APPLN. INFO.: US 2000-643642 A 20000822
WO 2001-EP9586 W 20010820

AB The present invention relates to a combination, esp. a pharmaceutical compn., comprising (a) an **insulin** secretion enhancer or a pharmaceutically acceptable salt thereof and (b) at least one of the active ingredients selected from the group consisting of (i) HMG-Co-A

reductase inhibitors or a pharmaceutically acceptable salt thereof; and (ii) ACE inhibitors or a pharmaceutically acceptable salt thereof; and, in case of a pharmaceutical compn., a pharmaceutically acceptable carrier. Formulations were given as examples, e.g., tablets contg. nateglinide.

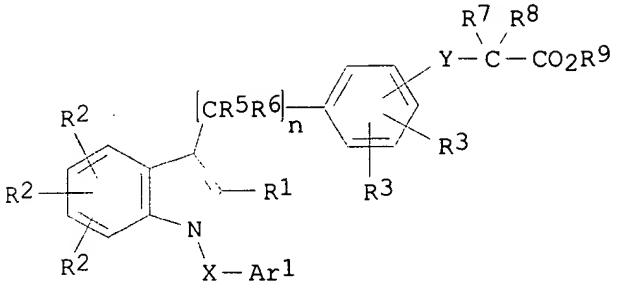
IT **9004-10-8, Insulin,** biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(combinations of **insulin** secretion enhancer, HMG-CoA reductase inhibitors and acetylcholinesterase inhibitors)

IT **1156-19-0, Tolazamide 10238-21-8, Glibenclamide 21187-98-4, Gliclazide 93479-97-1, Glimepiride 135062-02-1, Repaglinide 287714-41-4,** Rosuvastatin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combinations of **insulin** secretion enhancer, HMG-CoA reductase inhibitors and acetylcholinesterase inhibitors)

L38 ANSWER 10 OF 12 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:90008 HCAPLUS
DOCUMENT NUMBER: 136:151071
TITLE: Preparation of N-substituted indoles for treating **diabetes**
INVENTOR(S): Acton, John J., III; Black, Regina Marie; Jones, Anthony Brian; Wood, Harold Blair
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 73 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002008188	A1	20020131	WO 2001-US22979	20010720
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2002042441	A1	20020411	US 2001-912961	20010725

PRIORITY APPLN. INFO.: US 2000-220778P P 20000725
OTHER SOURCE(S): MARPAT 136:151071
GI



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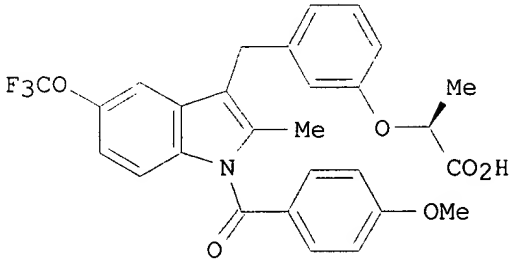


II

AB The title indoles having aryloxyacetic acid substituents [I; R1 = Me, optionally substituted with 1-3 F atoms; R2-R4 = H, halo, alkyl, etc.; R5, R6 = H, F, OH, alkyl; and R5 and R6 groups that are on the same carbon atom optionally may be joined to form a cyclopropyl group; R7, R8 = H, F, alkyl; or CR7R8 may form cycloalkyl; R9 = H, alkyl; Ar1 = (un)substituted Ph, naphthyl, pyridyl, quinolyl; X = CO, SO2, CH2, CHMe, CMe2, CF2, cyclopropylidene; Y = O, S; n = 0-5] which are agonists or partial agonists of PPAR gamma, and are useful in the treatment, control or prevention of non-**insulin** dependent **diabetes** mellitus (NIDDM), hyperglycemia, dyslipidemia, hyperlipidemia, hypercholesterolemia, hypertriglyceridemia, atherosclerosis, obesity, vascular restenosis, inflammation, and other PPAR mediated diseases, disorders and conditions, were prepd. E.g., a multi-step synthesis of (2S)-II was given.

IT **657-24-9, Metformin 56180-94-0, Acarbose 97322-87-7, Troglitazone 111025-46-8, Pioglitazone 122320-73-4, Rosiglitazone 147098-20-2,** ZD-4522 **161600-01-7, MCC-555**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of N-substituted indoles for treating **diabetes**)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

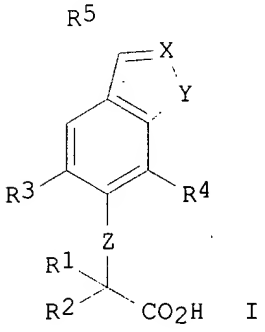
L38 ANSWER 11 OF 12 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:617987 HCAPLUS
DOCUMENT NUMBER: 135:180757
TITLE: Preparation of 1,2-benzoxazolyloxyacetic acids and analogs as PPAR agonists for treatment of **diabetes** and lipid disorders
INVENTOR(S): Liu, Kun; Xu, Libo; Jones, A. Brian
PATENT ASSIGNEE(S): Merck + Co. Inc., USA

SOURCE: PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001060807	A1	20010823	WO 2001-US4636	20010214

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-183593P P 20000218
OTHER SOURCE(S): MARPAT 135:180757
GI



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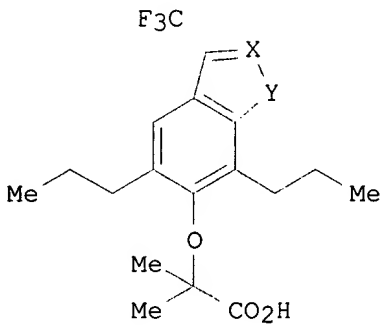

II

AB The title compds. (I) [wherein R1 and R2 = independently H, F, (halo)alkyl, (halo)alkenyl, (halo)alkynyl; or R1 and R2 may form a cycloalkyl group; R3 and R4 = independently (fluoro)alkyl, (fluoro)alkenyl, (fluoro)alkynyl, or Cl; X = N or CR; Y = O, S, nor NR; Z = O or S; R = independently H or optionally fluoro- or alkoxy-substituted (cyclo)alkyl(oxy), alkenyl(oxy), or alkynyl(oxy); R5 = H or (un)substituted alkyl, alkenyl, alkynyl, (hetero)aryl(oxy), heterocyclyl(oxy), etc.; and pharmaceutically acceptable salts and prodrugs thereof] were prepd. For example, 2,4-dihydroxy-3,5-dipropyl-1',1',1'-trifluoroacetophenone oxime was acetylated and then treated with pyridine and TEA to give 5,7-dipropyl-6-hydroxy-3-trifluoromethyl-1,2-benzisoxazole. Etherification with Me .alpha.-bromoisobutyrate in the presence of Cs2CO3 in DMF, followed by sapon., afforded the 1,2-benzoxazolyloxyacetic acid (II). I are potent agonists of peroxisome proliferator activated receptor (PPAR) .alpha. and/or .gamma. and are useful in the treatment, control, or prevention of non-**insulin** dependent **diabetes** mellitus (NIDDM), hyperglycemia, dyslipidemia, hyperlipidemia, hypercholesterolemia, hypertriglyceridemia,

atherosclerosis, obesity, vascular restenosis, inflammation, and other PPAR.alpha. and/or .gamma. mediated diseases, disorders, and conditions (no data).

IT **657-24-9, Metformin 9004-10-8, Insulin**
, biological studies **9004-10-8D, Insulin**, mimetics, biological studies **56180-94-0, Acarbose 97322-87-7, Troglitazone 111025-46-8, Pioglitazone 122320-73-4, Rosiglitazone 147098-20-2**, ZD-4522 **161600-01-7, MCC-555**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(coadministration with; prepn. of benzisoxazolyloxyacetic acid PPAR agonists via cyclization of dihydroxyacetophenone oximes for treatment of **diabetes** and lipid disorders)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 12 OF 12 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:553418 HCAPLUS
DOCUMENT NUMBER: 133:144931
TITLE: Use of 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitors for the manufacture of a medicament for the treatment of **diabetic** neuropathy
INVENTOR(S): Cameron, Norman Eugene; Cotter, Mary Anne
PATENT ASSIGNEE(S): Astrazeneca UK Limited, UK; University Court of the University of Aberdeen
SOURCE: PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000045818	A1	20000810	WO 2000-GB280	20000201
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
BR 2000007996	A	20011030	BR 2000-7996	20000201
EP 1150678	A1	20011107	EP 2000-901744	20000201
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002536332	T2	20021029	JP 2000-596938	20000201
NO 2001003812	A	20011002	NO 2001-3812	20010803

PRIORITY APPLN. INFO.:
GB 1999-2591 A 19990206
GB 1999-2594 A 19990206
WO 2000-GB280 W 20000201

AB The invention relates to a new use of a statin drug in the improvement of **diabetic** neuropathy, specifically in improving nerve conduction velocity and nerve blood flow in patients suffering **diabetes**, in

particular to pharmaceutical combinations of the statin drug and other agents known to improve **diabetic** neuropathy such as an aldose reductase inhibitor, an angiotensin converting enzyme inhibitor, or an angiotensin II antagonist, which combinations are useful in the prevention and treatment of the complications of **diabetes**.

IT **657-24-9, Metformin 1156-19-0, Tolazamide 9004-10-8, Insulin**, biological studies **10238-21-8, Glibenclamide 21187-98-4, Gliclazide 56180-94-0, Acarbose 93479-97-1, Glimepiride 97322-87-7, Troglitazone 111025-46-8, Pioglitazone 122320-73-4, Rosiglitazone 135062-02-1, Repaglinide 147098-20-2 161600-01-7, MCC-555 287714-41-4**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(HMG-CoA reductase inhibitors for treatment of **diabetic** neuropathy, and combinations with other agents)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT